
Generation of Induced Neuronal Cells by the Single Reprogramming Factor ASCL1.

Journal: Stem Cell Reports

Publication Year: 2014

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PubMed link: 25254342

Funding Grants: Stanford CIRM Training Program

Public Summary:

Scientific Abstract:

Direct conversion of nonneural cells to functional neurons holds great promise for neurological disease modeling and regenerative medicine. We previously reported rapid reprogramming of mouse embryonic fibroblasts (MEFs) into mature induced neuronal (iN) cells by forced expression of three transcription factors: ASCL1, MYT1L, and BRN2. Here, we show that ASCL1 alone is sufficient to generate functional iN cells from mouse and human fibroblasts and embryonic stem cells, indicating that ASCL1 is the key driver of iN cell reprogramming in different cell contexts and that the role of MYT1L and BRN2 is primarily to enhance the neuronal maturation process. ASCL1-induced single-factor neurons (1F-iN) expressed mature neuronal markers, exhibited typical passive and active intrinsic membrane properties, and formed functional pre- and postsynaptic structures. Surprisingly, ASCL1-induced iN cells were predominantly excitatory, demonstrating that ASCL1 is permissive but alone not deterministic for the inhibitory neuronal lineage.

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